PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference ABL-026-PCT	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/EP2006/000273	International filing date *(day/month/year)* 13.01.2006	Priority date *(day/month/year)* 14.01.2005
International Patent Classification (IPC) or national classification and IPC INV. G01N33/68 G01N33/86		
Applicant ABLYNX N.V. et al.		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 7 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☒ *sent to the applicant and to the International Bureau)* a total of 5 sheets, as follows:
      ☒ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☒	Box No. VII	Certain defects in the international application
☒	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
14.11.2006	05.02.2007
Name and mailing address of the international preliminary examining authority: European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized officer Lunter, Pim Telephone No. +31 70 340-8908

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/EP2006/000273

Box No. I Basis of the report

1. With regard to the **language**, this report is based on

   ☒ the international application in the language in which it was filed

   ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3(a) and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4(a))
   - ☐ international preliminary examination (under Rules 55.2(a) and/or 55.3(a))

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages	
1-34	as originally filed
Claims, Numbers	
1-23	filed with the demand
Drawings, Sheets	
1/8-8/8	as originally filed

   ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	18-19
	No:	Claims	1-17,20-23
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-23
Industrial applicability (IA)	Yes:	Claims	1-23
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Reference is made to the following documents:

D1 Murdock et al., Thromb Haemost 78, 1272-1277 (1997)
D2 Favaloro et al., Thromb Haemost 84, 541-547 (2000)
D3 Favaloro et al., Am J Clin Path 114, 608-618 (2000)
D4 WO 01/02853
D5 Veyradier et al., Int J Clin Lab Res 28, 201-210 (1998)
D6 Vanhoorelbeke et al., Thromb Haemost 83, 107-113 (2000)
D7 Favaloro et al., Blood Coag Fibrinolysis 2, 285-291 (1991)
D8 Tsai et al., New Eng J Med 339, 1585-1594 (1998)
D9 Lattuada et al., Haematologica 88, 1029-1034 (2003)
D10 WO 2004/062551
D11 WO 00/24781

Re Item I
Basis of the report

1 The amendments meet the requirements of Article 34 PCT.

Re Item V
Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1 The present application does not meet the requirements of Article 33(2) PCT as claims 1-17 and 20-23 are not novel.

2 The subject-matter of independent claim 1 is anticipated by D1-D9, which disclose methods of distinguishing between states or forms of von Willebrand disease (vWD) subtypes, thrombotic thrombocytopenic purpura (TTP) (D8, whole document) and HELLP syndrome (D9, whole document), using reagents that specifically bind von Willebrand Factor (vWF) in the active conformation (i.e. having an exposed A1 domain) in the presence of vWF in the inactive conformation (see e.g. D1, page 1272, right column; D2, page 541; D3, page 608, right column; D4, page 2-12; and other documents cited on the International Search Report). D1-D3 disclose the use of

antibodies that specifically recognize vWF in the active conformation for the differentiation of vWD subtypes. Thus, the subject-matter of independent claims 1 and 23 is not novel (Article 33(2) PCT).

3 The subject-matter of independent claim 22 is anticipated by documents D1-D4, D6-7 and D10-D11, which disclose binding agents for activated vWF and kits containing them (D10, page 3, page 7-8; D11, page 2-3). Thus, the subject-matter of independent claim 21 is not novel.

4 Even if the objections noted above could be overcome, the present application would not meet the requirements of Article 33(3) PCT as claims 1-23 do not involve an inventive step.

5 Independent claims 1 and 23 recite a method for distinguishing between different states or forms of diseases characterized by thrombocytopenia and/or spontaneous interaction between vWF and platelets, and the use of an antibody specifically recognizing activated vWF in such a method, respectively. Independent claim 22 recites a kit for determining vWF amounts.

6 Thus, the problem this application addresses is therefore how to provide an alternative assay to distinguish between different states or forms of diseases characterized by thrombocytopenia and/or spontaneous interaction between vWF and platelets. The solution is to use an antibody specifically recognizing active vWF in the presence of inactive vWF.

7 The solution cannot be regarded as inventive as it represents obvious alterations from those in D1-D11 which are well within the knowledge and abilities of the skilled person.

8 Dependent claims 2-21 do not appear to contain any additional features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT with respect to novelty or inventive step as the subject matter of said claims is either disclosed in the cited prior art or also falls within the knowledge and ability of the skilled person (D1-D11).

9 All claims meet the requirement of Article 33(4) PCT as they are industrially applicable.

Re Item VII

Certain defects in the international application

1 Documents D1-D9 and D11 are not mentioned in the description (Rule 5.1(a) (ii) PCT).

2 Independent claims 1, 22 and 23 are not drafted in the two-part form (Rule 6.3. PCT).

Re Item VIII

Certain observations on the international application

1 The present application does not meet the requirements regarding clarity, disclosure and support for the following reasons (Article 5/6 PCT).

2 Independent claims 1 and 23 recite a method and a use of an antibody for distinguishing different states or forms of diseases characterized by thrombocytopenia and/or spontaneous interaction between vWF and platelets. The methods are merely exemplified by studies on vWD type 2B, TTP and HELLP syndrome. The skilled person would therefore not be able to find threshold values of activated vWF for other diseases without inventive skill or undue experimentation. Thus, the scope of the claims are broader than is justified by the contribution to the art.

3 Independent claim 1 lacks essential technical features as it does not recite which ranges of activated vWF correlate with the "different states or forms of the disease or disorder".

4 Independent claim 21 is unclear due to usage of the term "one or more parts,

elements or components of kits for binding assays known per se" and the term "...an agent that binding agent...".